Infection Related Glomerulopathy

Introduction – Rapid Overview

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Mansoura University – September 2014

At the beginning of the last century:
Postulated that the disease resulted from antibodies that instead of having beneficial effects were pathogenic, an insight that constitutes a landmark that opened the field of immune-mediated renal disease.1

Clemens von Pirquet

Table 21 | Infections associated with glomerulonephritis

Bacterial
Mycobacterium leprae, M. tuberculosis
Treponema pallidum
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Streptococcus pneumoniae, S. virdans, S. pyogenes
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Coxiella burnettii[a]
Brucella abortus[a]
Listeria monocytogenes[a]

- Post-streptococcal GN
- Endocarditis associated GN
- Shunt nephritis

Fungal
Histoplasma capsulatum[a]
Candida[a]
Coccidiodes immitis[a]

Protozoal
Plasmodium malariae, P. falciparum
Leishmania donovani
Toxoplasma gondii
Trypanosoma cruzi, T. bruci
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Brugia malayi
Loa loa
Onchocerca volvulus
Trichinella spiralis[a]

ECHO, enteric cytopathic human orphan; GN, glomerulonephritis.
[a]Only case reports documented.

Post-streptococcal Glomerulonephritis

Nephritogenic strains of **group A *Streptococcus pyogenes***

	PIGN	IgA Nephropathy
Timing in relation-ship to a URI	10–14 days or more after the onset	"Synchronous" with the URI
Gross hematuria	30%–50%	>80%
Nephrotic syndrome	10%–20%	5%–10%
Hypertension	>80%	30%–50%

Nephritis

Poynard T, Yuen MF, Ratziu V et al. Viral hepatitis C. Lancet 2003; 362:2095–2100.

Post-streptococcal Glomerulonephritis

Pathogenesis

Streptococcal Infection

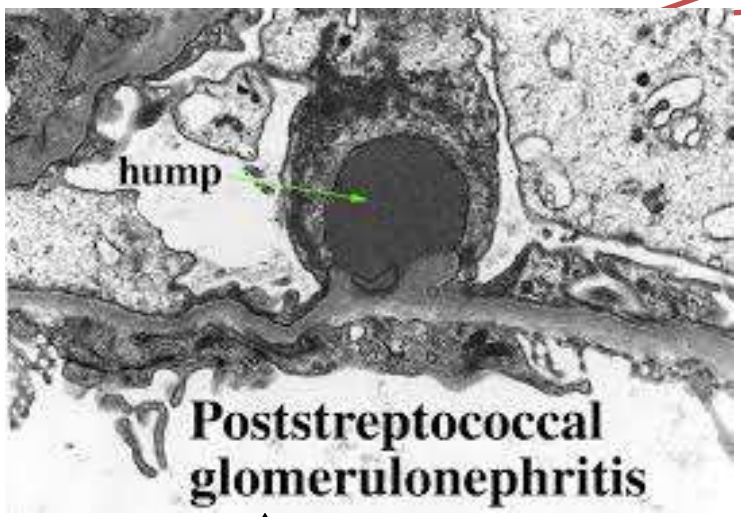
Streptococcal proteinase exotoxin B (SPEB)

Development of circulating immune complexes

Deposited subendothelial and mesangial locations

Initiate an inflammation (local complement activation and the recruitment of neutrophils and monocytes macrophages)

Cationic antigens or dissociation of immune complexes into the outer aspect of the glomerular basement membrane



Post-streptococcal Glomerulonephritis

Pathogenesis

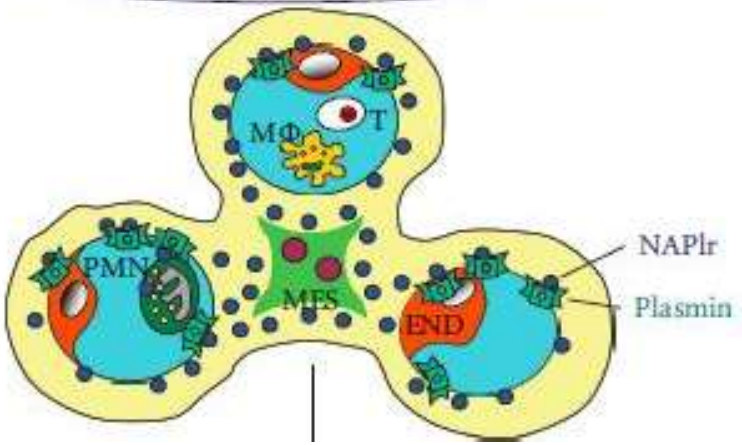
Nephritis-associated plasmin receptor (NAPLr)

Streptococcal Infection

Streptococcal proteinase exotoxin B (SPEB)

Development of circulating immune complexes

Deposition of NAPlr on the inner side of glomerular tufts, inducing plasmin-related endocapillary inflammation



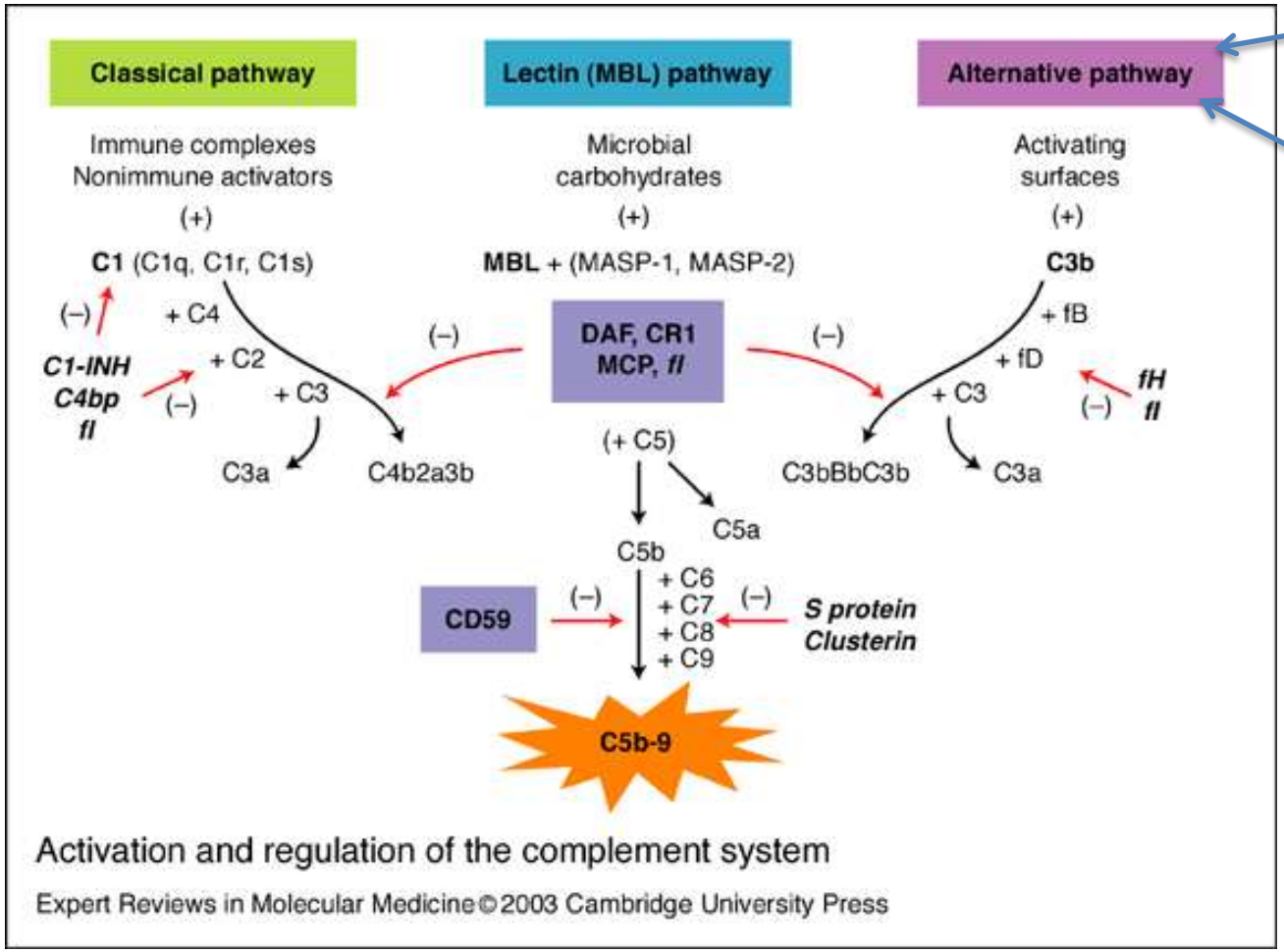
A local direct mechanism of glomerular inflammatory damage

it is not co-localized with complement or immunoglobulin

Post-streptococcal Glomerulonephritis

Complement Activation

Low C3 / Normal or slightly low C4



Activation and regulation of the complement system

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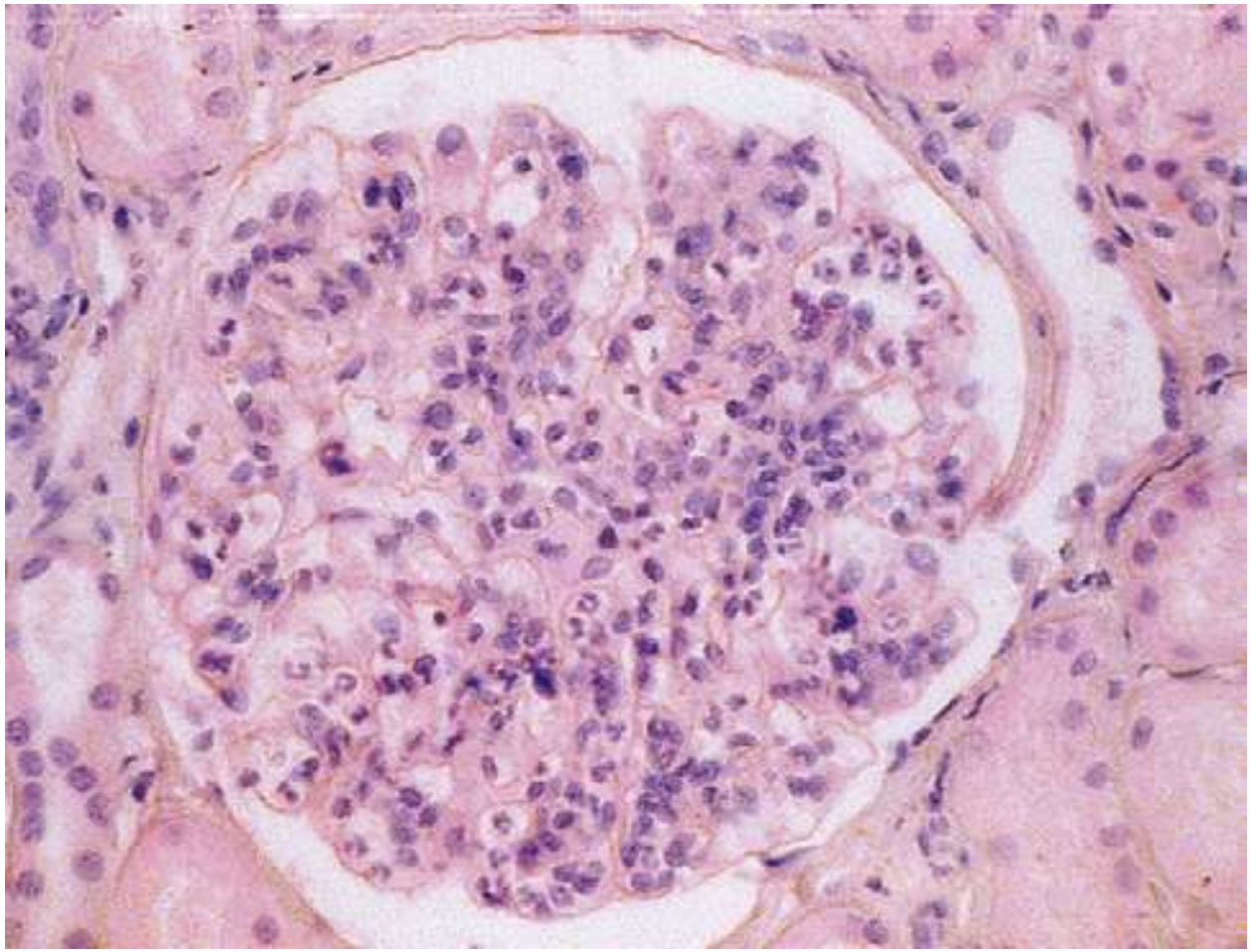
NAPLr

C3Nef IgG antibodies in sera

Post-streptococcal Glomerulonephritis

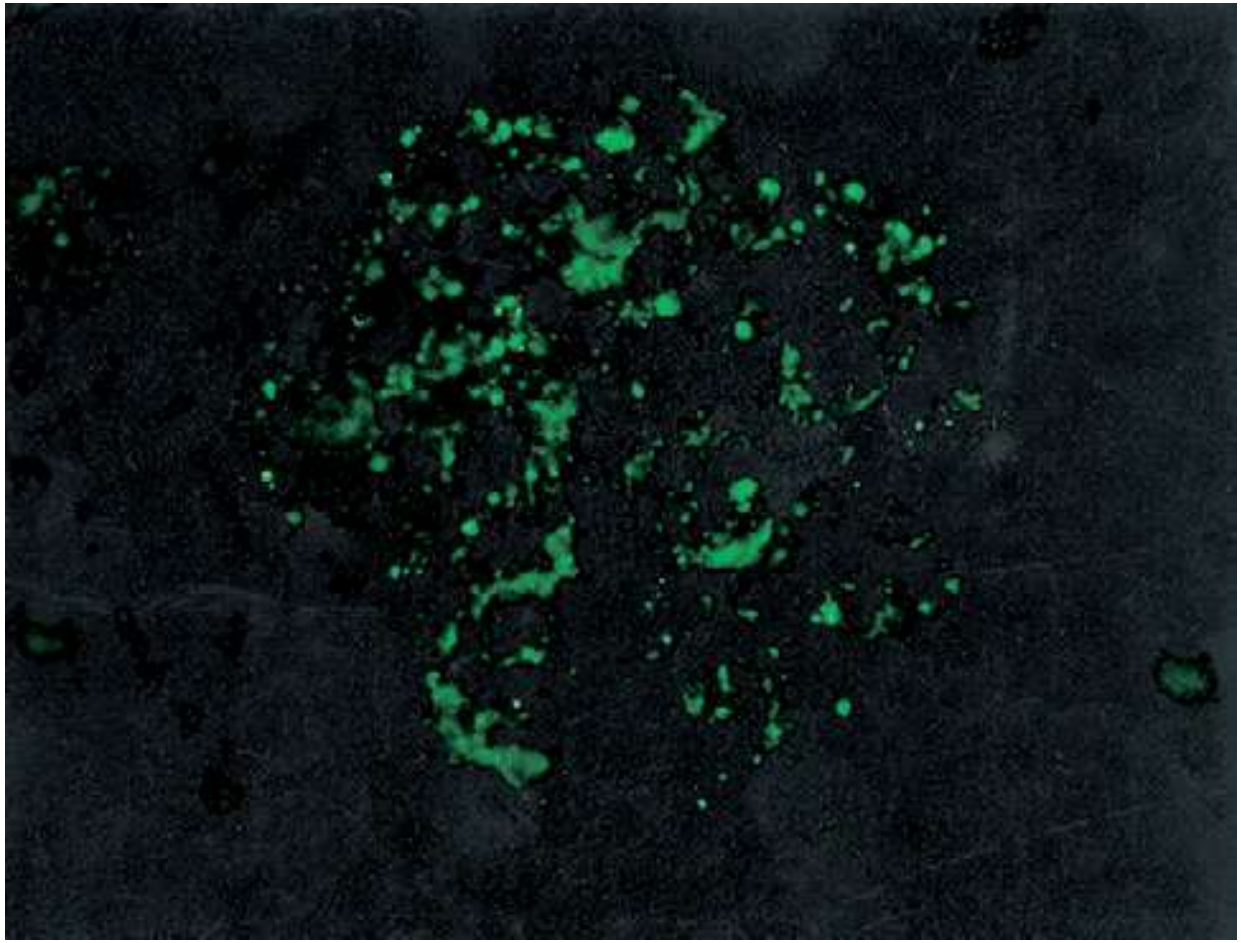
Pathology



Diffuse endocapillary GN with proliferation of mesangial and endothelial cells

Post-streptococcal Glomerulonephritis

Pathology



Glomerular immune deposits of C3 (100% of the cases), IgG (62%), IgM (76%)

Post-streptococcal Glomerulonephritis Management

9.1: For the following infection-related GN, we suggest appropriate treatment of the infectious disease and standard approaches to management of the kidney manifestations: (*2D*)

- poststreptococcal GN;
- infective endocarditis-related GN;
- shunt nephritis.

Post-streptococcal Glomerulonephritis

Management

Pulses of i.v. methylprednisolone can be considered in patients with extensive glomerular crescents and rapidly progressive GN, based on extrapolation from other rapidly progressive and crescentic GNs, although there is no evidence from RCTs.

Post-streptococcal Glomerulonephritis
Important Clinical Points

If decreased C3 levels lasted for more than a month (suggests lupus or hypocomplementemic MPGN)

Mild proteinuria (<500 mg/day) and microscopic hematuria may persist for up to 1 year

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Endocarditis-Associated Glomerulonephritis

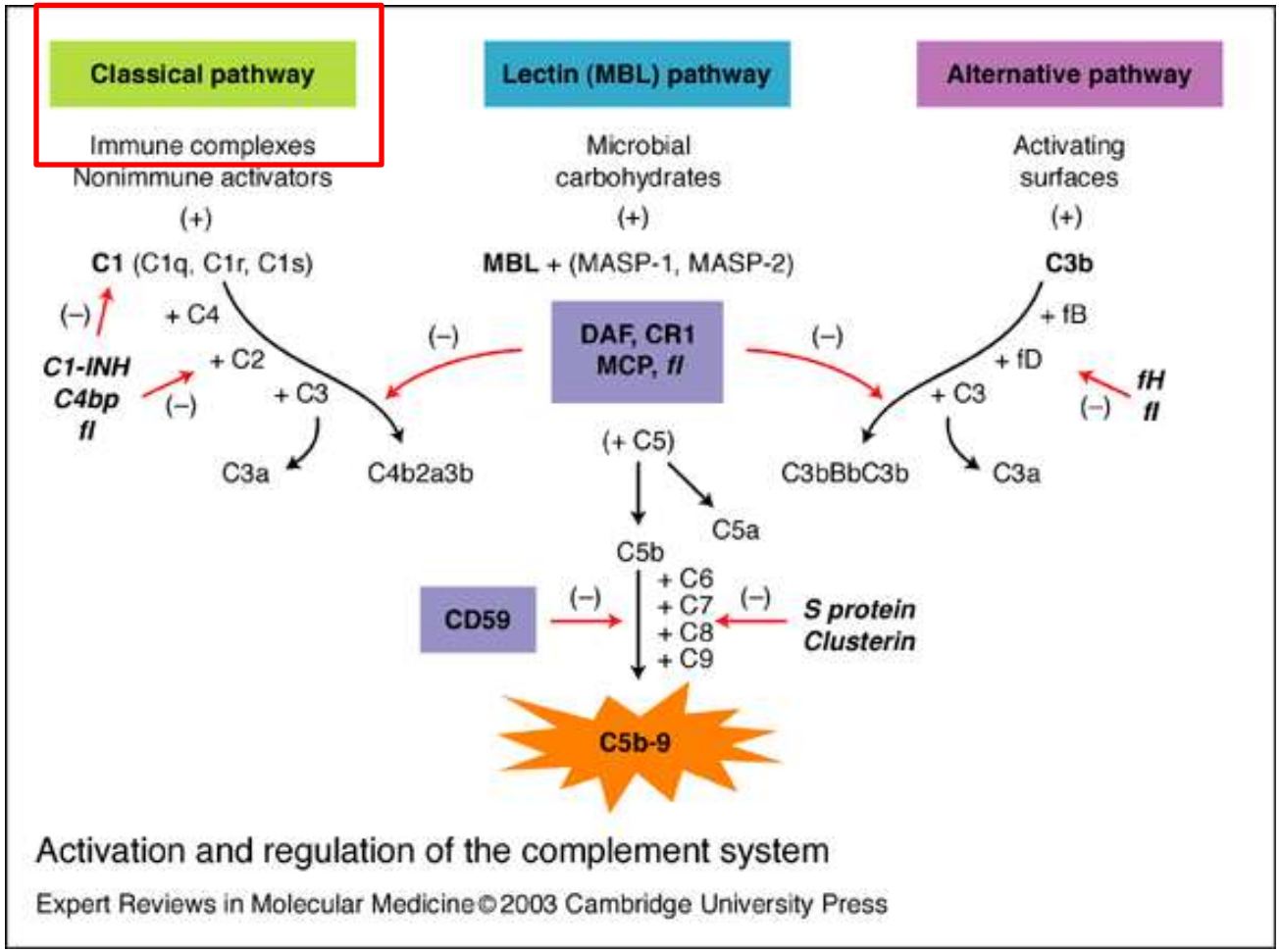
Pathogenesis

Deposition of immune complexes containing bacterial antigens in glomeruli, a mechanism similar to that proposed for PSGN.

Endocarditis-Associated Glomerulonephritis

Complement Activation

Low C3 / low C4



Activation and regulation of the complement system

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Endocarditis-Associated Glomerulonephritis

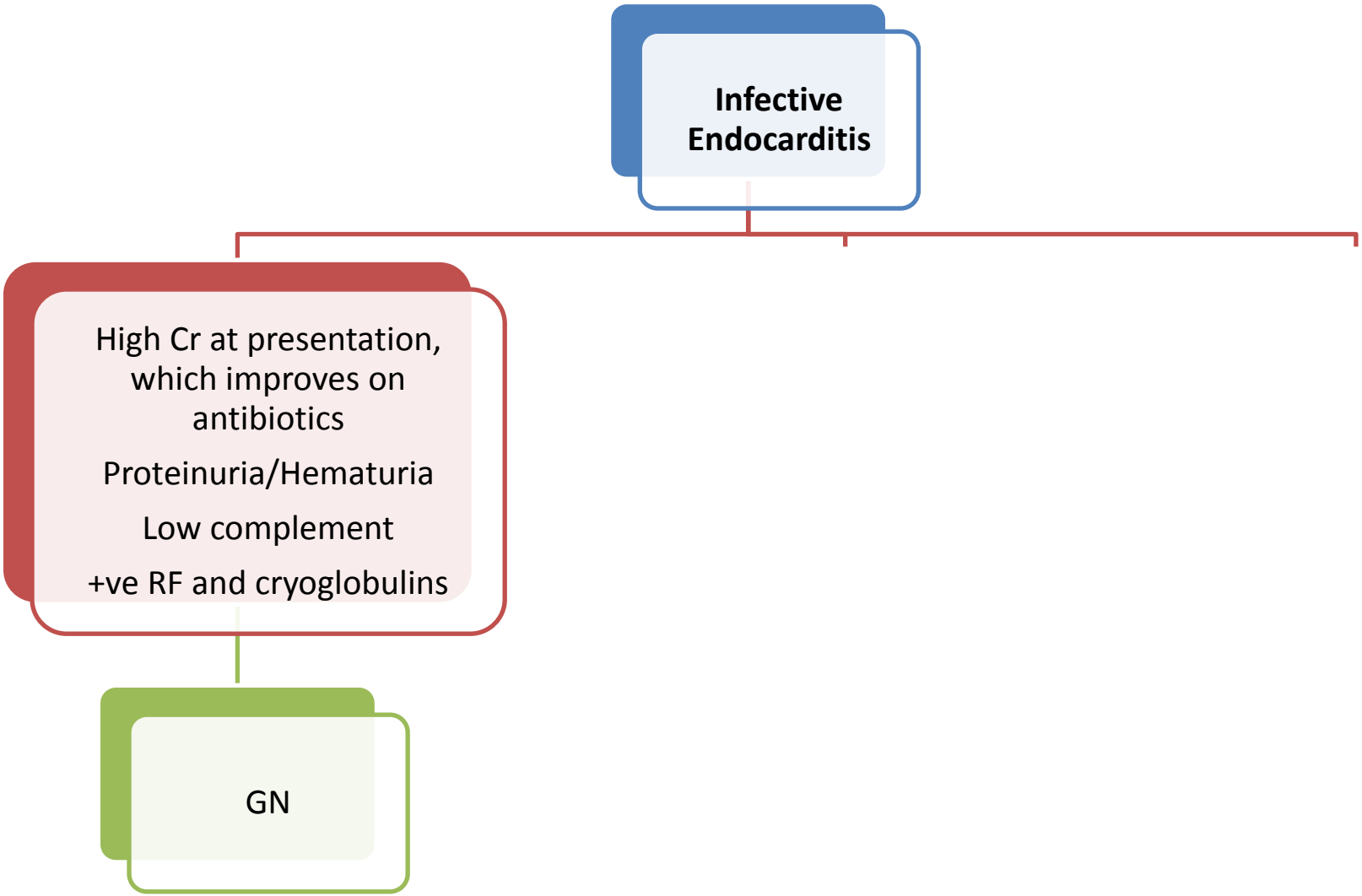
Pathology

Renal Syndromes Associated with Infection			
Clincical Presentation	**Time Course**	**Pathologic Findings**	**Examples**
Subclinical, microhematuria non-nephrotic proteinuria	Acute	Mesangioproliferative GN	Typhoid fever, *Pl. falciparum* PSGN
Acute nephritic syndrome	Acute	Diffuse proliferative GN	PSGN
Acute renal failure, nephrotic syndrome	Acute, chronic	Diffuse proliferative GN, cresents 1. IgM, IgG dominant 2. IgA dominant	 1. Endocarditis, PSGN 2. Methicillin-resistant *S. Aureus*
Nephrotic syndrome reduced GFR	Chronic	1. MPGN type I ± cryoglobulins 2. Focal segmental glomerulosclerosis	1. Hepatitis C virus, infected AV shunts 2. HIV, parvovirus
Nephrotic syndrome	Chronic	1. Membranous nephropathy 2. Amyloid	1. Hepatitis B virus 2. Leprosy, *Schistosoma*, kala-azar
Acute renal failure, systematic symptoms, arthralgias, skin ulcers	Acute, chronic	Vasculitis, crescents, tubulointerstitial inflammation, atrophy and fibrosis	Hepatitis B virus, HIV
Hemplytic-uremic syndrome	Acute	Arteriolar thickening and occlusion, microthrombi, capillary wall thickening	*E. coli* O157-H7
Azotemia, non-nephrotic proteinuria, eosinophillia	Acute, chronic	Interstitial nephritis	Epstein-Barr virus, legionnaire's disease, Hantavirus, kala-azar

Less commonly: focal GN, MN, and MPGN type I may be found.

Endocarditis

Renal Presentation (other than GN)



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- infective endocarditis-related GN;
- shunt nephritis.

Endocarditis-Associated Glomerulonephritis

Management

In cases with crescentic GN, pulse corticosteroid therapy and plasma exchange have been used in addition to effective antibiotic therapy, but the value of these treatments remains undefined.

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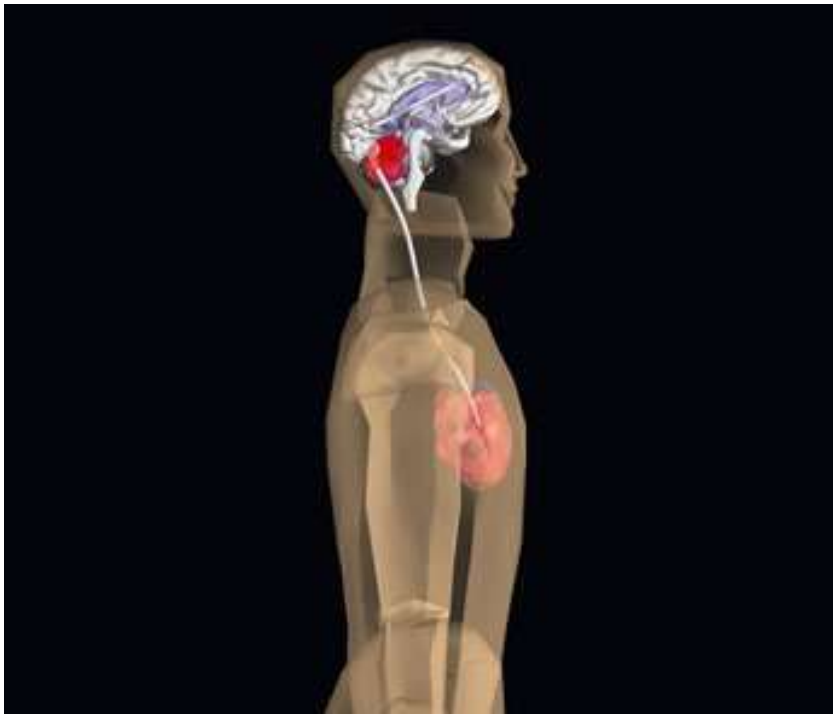
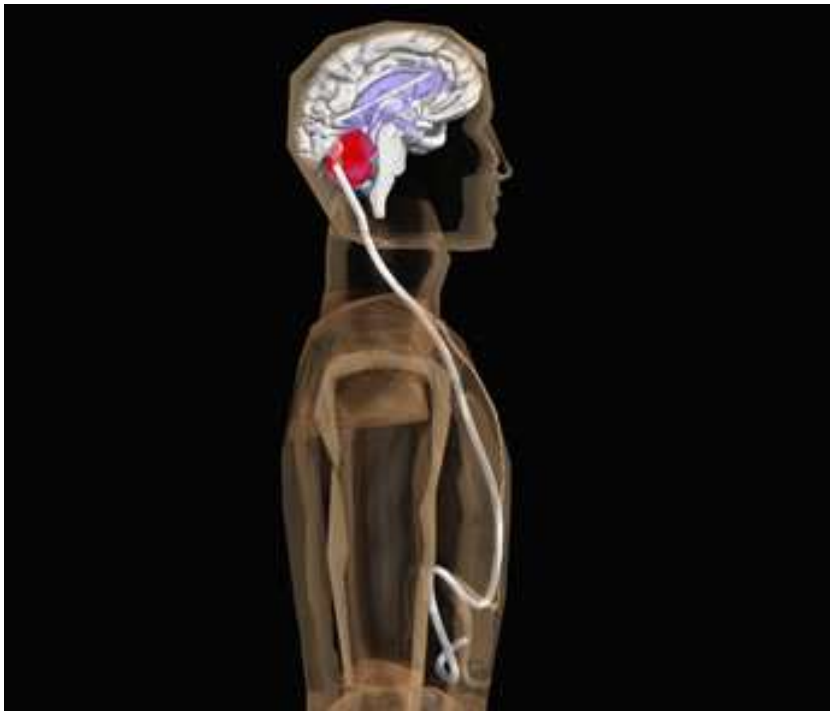
Shunt Nephritis



Infected atrioventricular shunts; this may occur 2 months to many years after insertion

- S. Epidermidis and S. aureus
- Less frequently Propionibacterium acnes, diphtheroids, Pseudomonas, or Serratia.

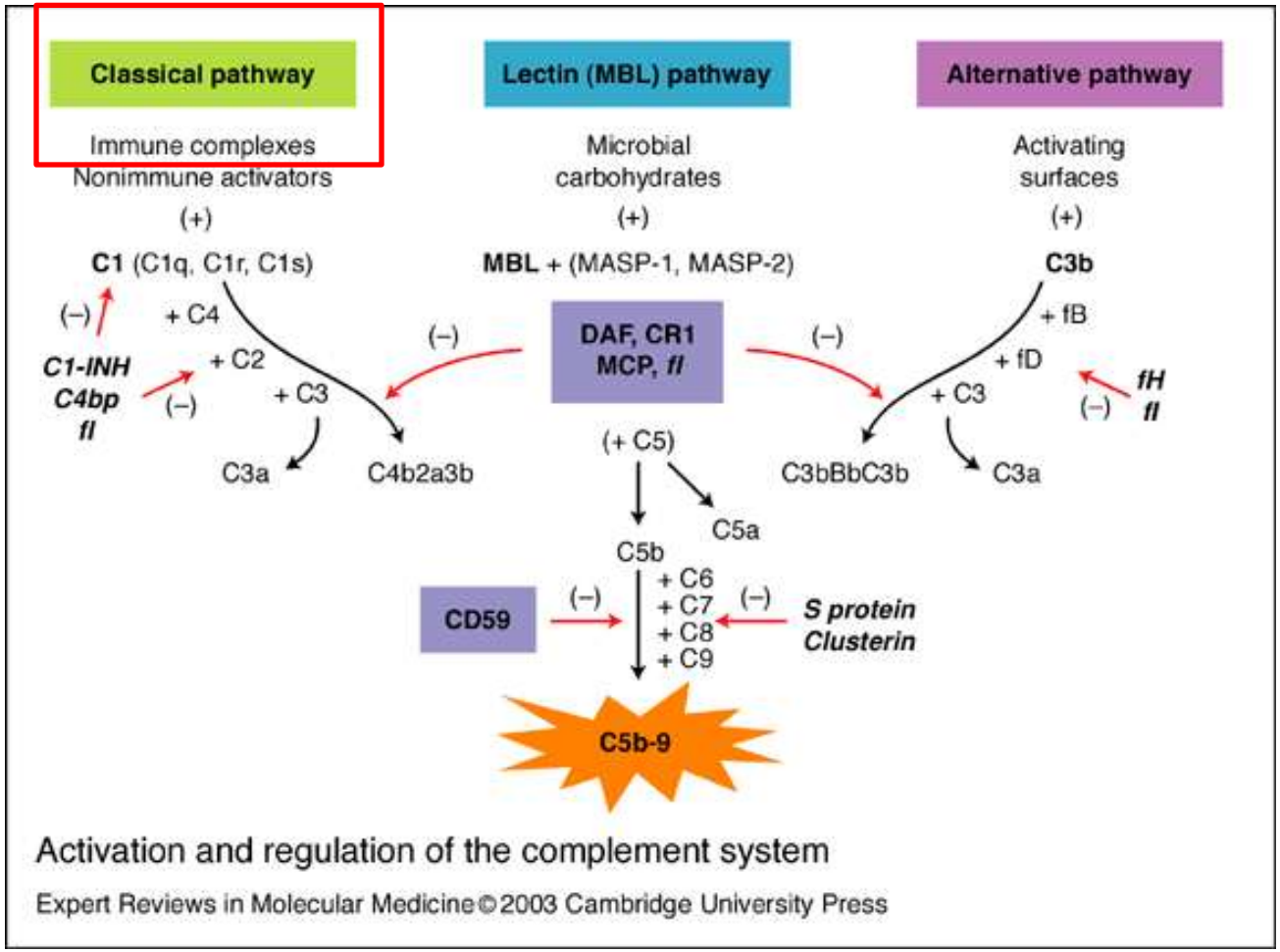


ventriculoperitoneal shunts are rarely complicated with GN.

Shunt Nephritis

Complement Activation

Low C3 / low C4



Activation and regulation of the complement system

Shunt Nephritis
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IgM, IgG, and C3 deposits are present in the glomerular capillary and mesangium.

Shunt Nephritis Management

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prompt removal of the infected atrioventricular shunt, which is usually replaced by a ventriculoperitoneal shunt.

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Viral
Hepatitis B and C
Human immunodeficiency virus
Epstein-Barr virus
Coxsackie B
ECHO virus
Cytomegalovirus
Varicella zoster
Mumps
Rubella
Influenza

Helminthic
Schistosoma mansoni, S. japonicum, S. haematobium
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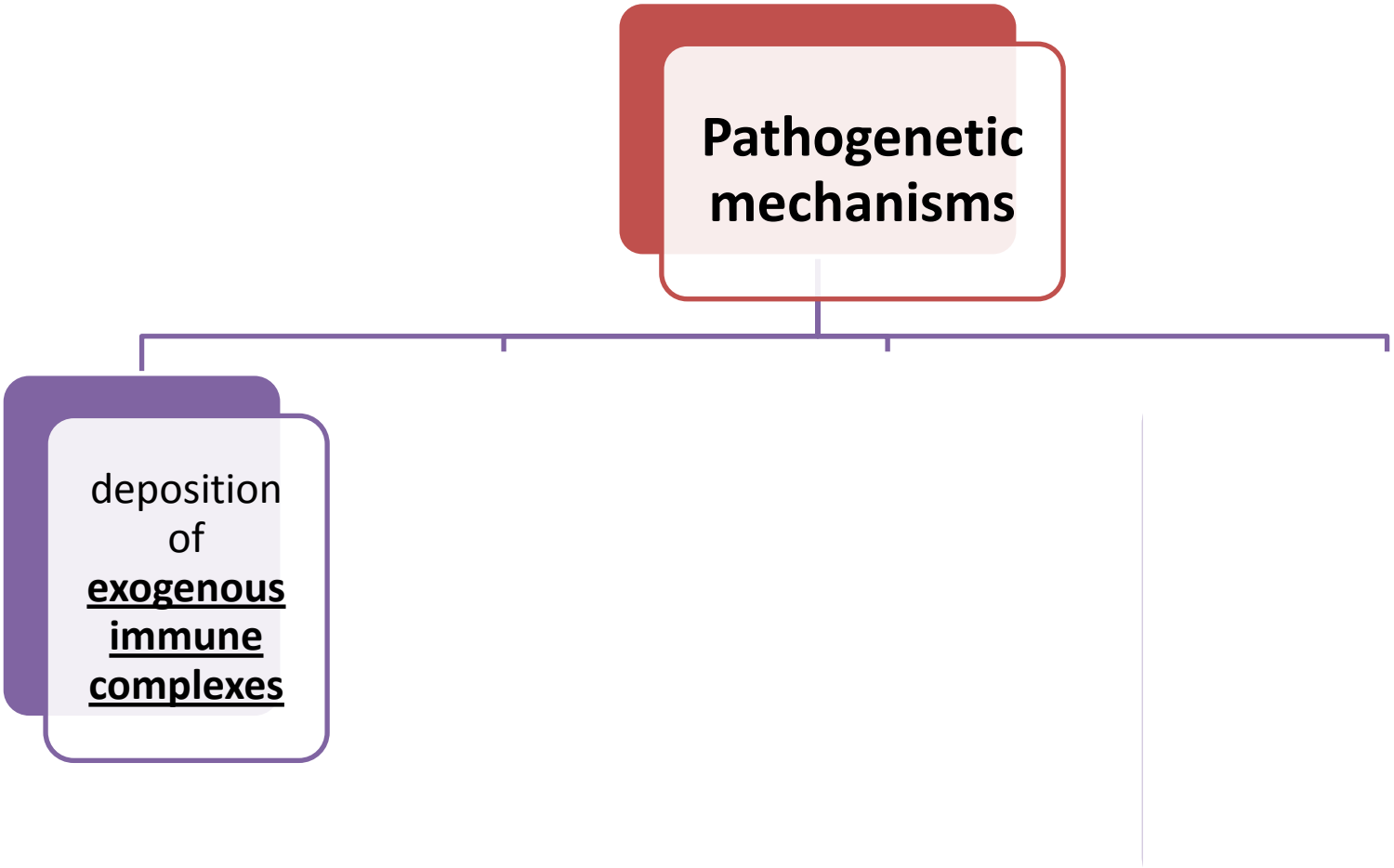
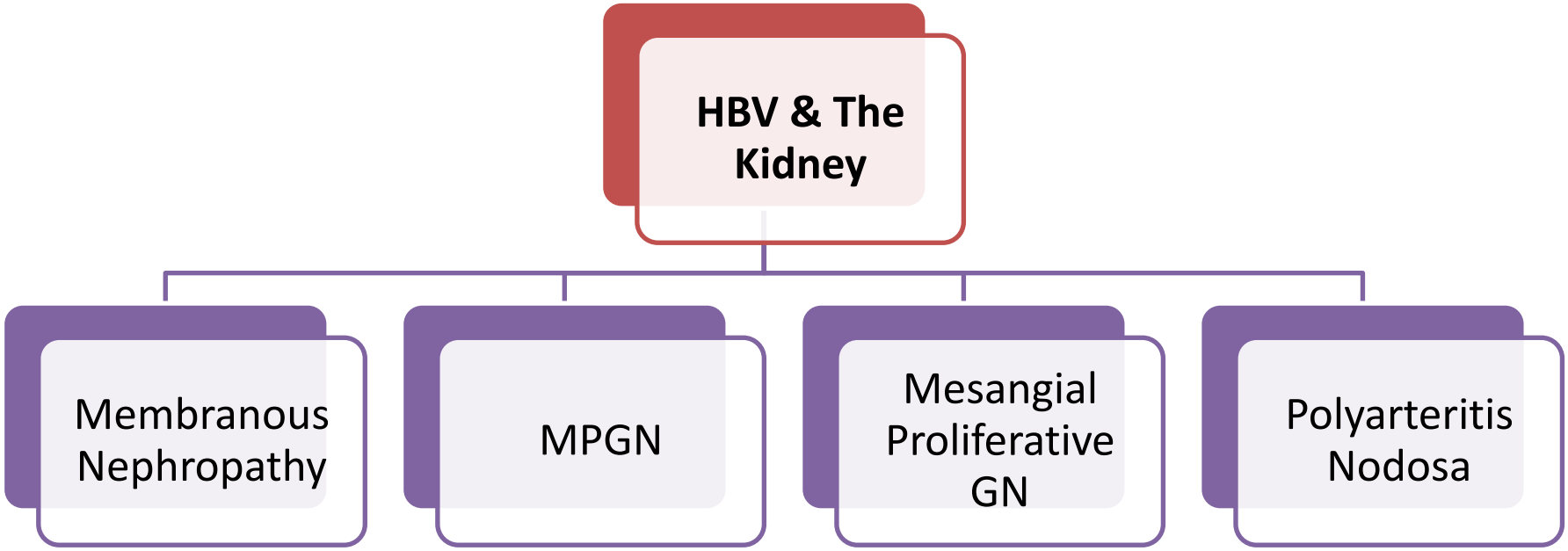
Viral Infection Related Glomerulopathy

General Pathogenesis



Hepatitis B Virus–Associated Renal Disease



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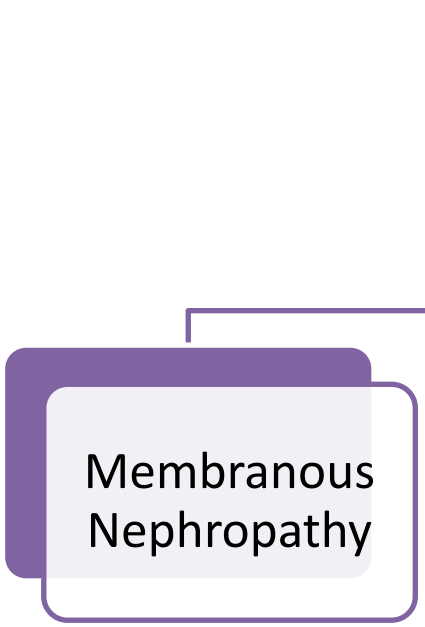
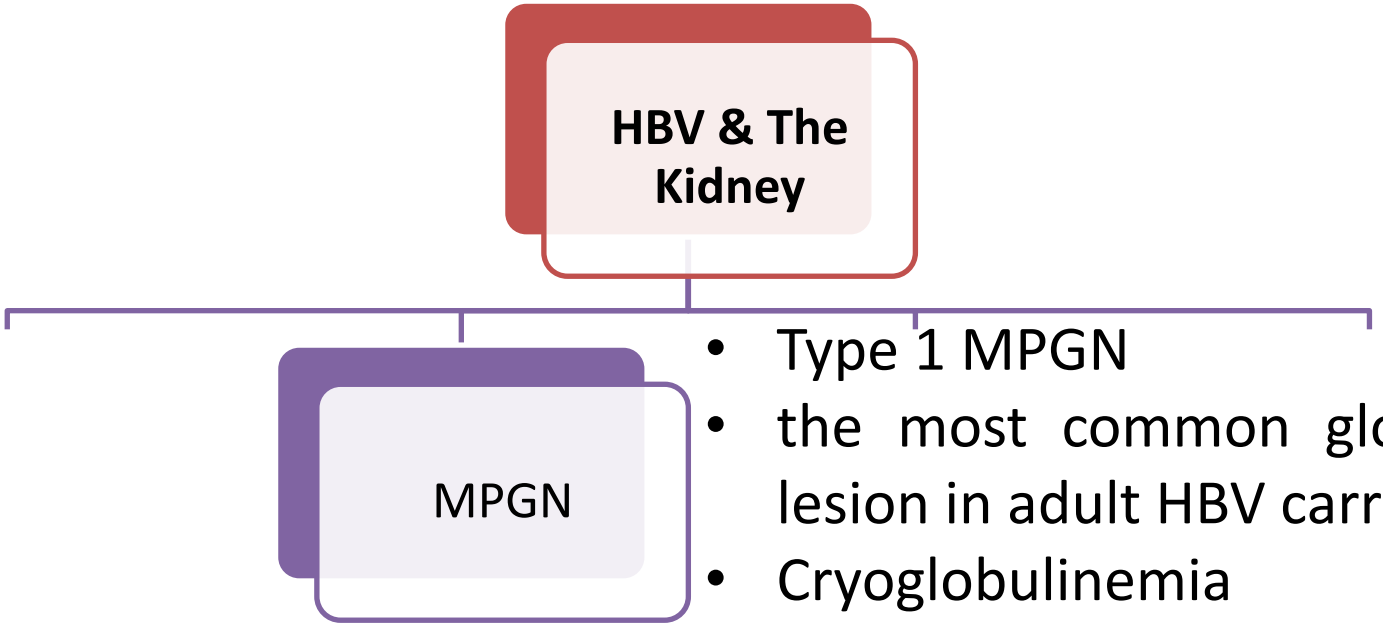


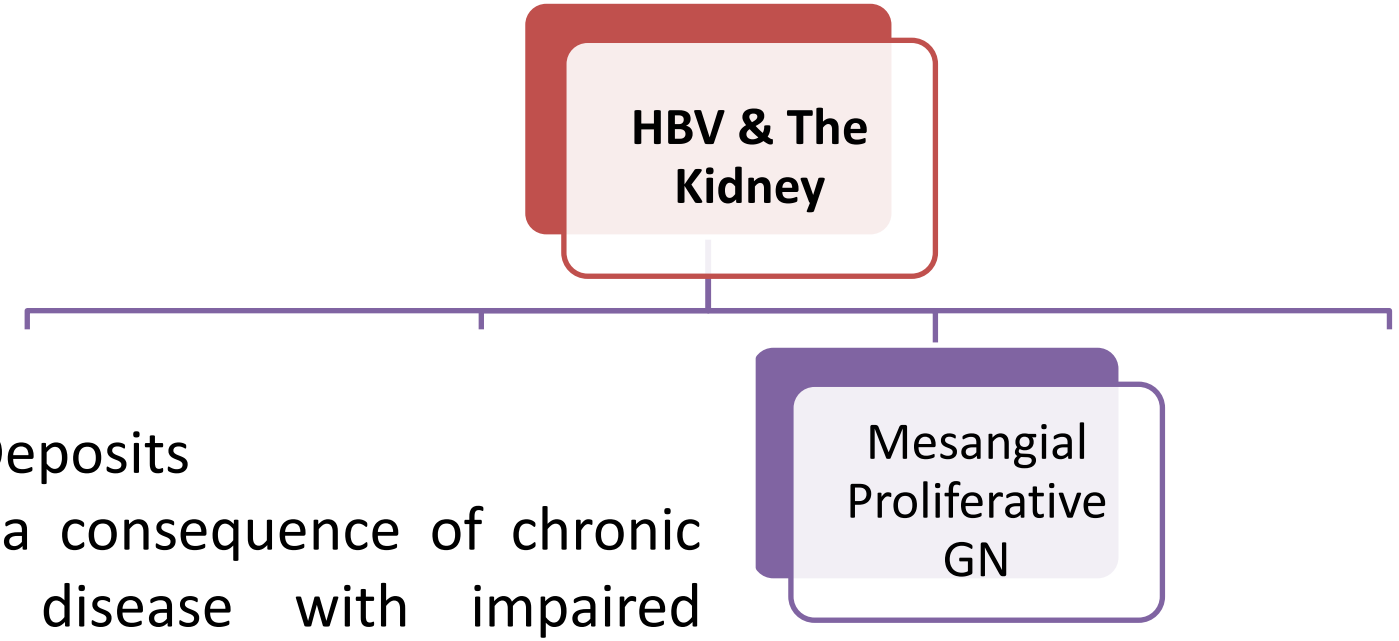
- MN may occur in chronic HBV carriers
- Nephrotic
- Often have impaired renal function
- Clinically apparent liver disease
- C3 and C4 levels are decreased in 20% to 50%
- Mesangial immune deposits may also be present

Hepatitis B Virus–Associated Renal Disease



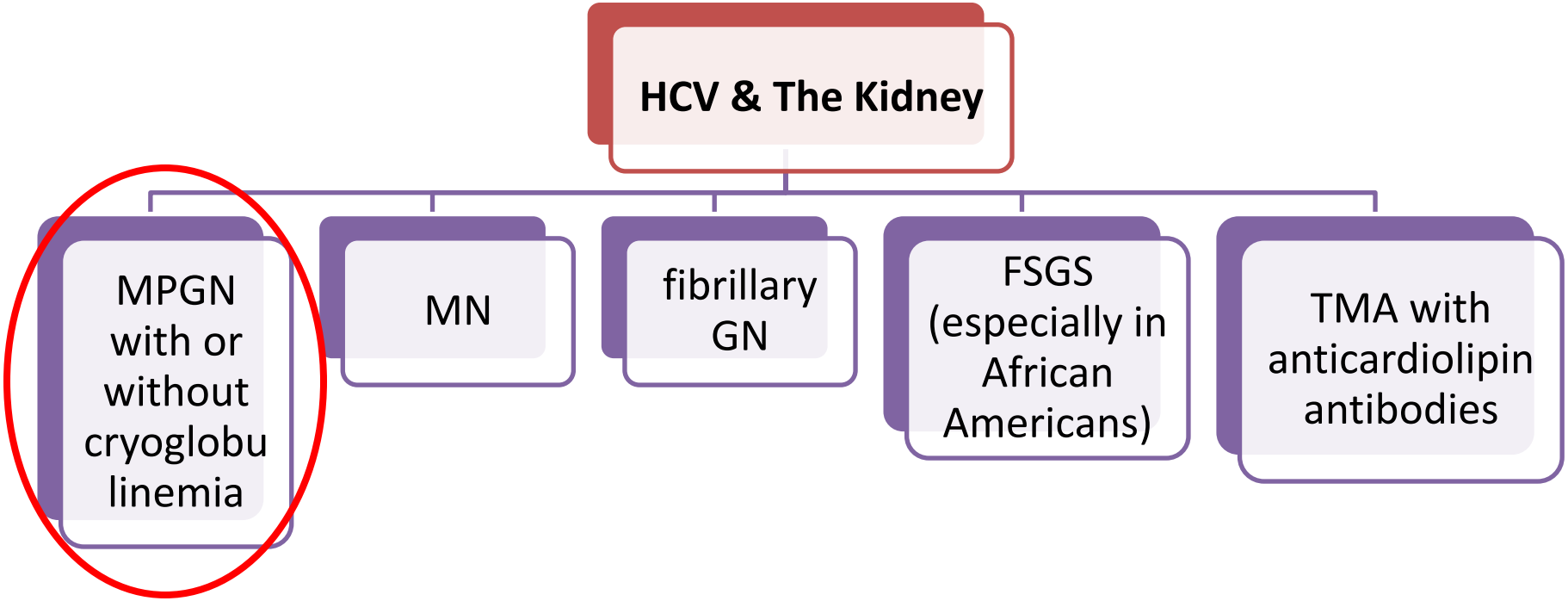
- Type 1 MPGN
- the most common glomerular lesion in adult HBV carriers
- Cryoglobulinemia
- Chronic liver disease (may be clinically asymptomatic)
- Nephrotic or non nephrotic proteinuria, often associated with microhematuria

Hepatitis B Virus–Associated Renal Disease



- IgA Deposits
- It is a consequence of chronic liver disease with impaired clearance of IgA circulating immune complexes

Hepatitis C Virus–Associated Renal Disease



Hepatitis C Virus–Associated Renal Disease

Hepatitis C Virus–Associated Renal Disease

Complement Activation

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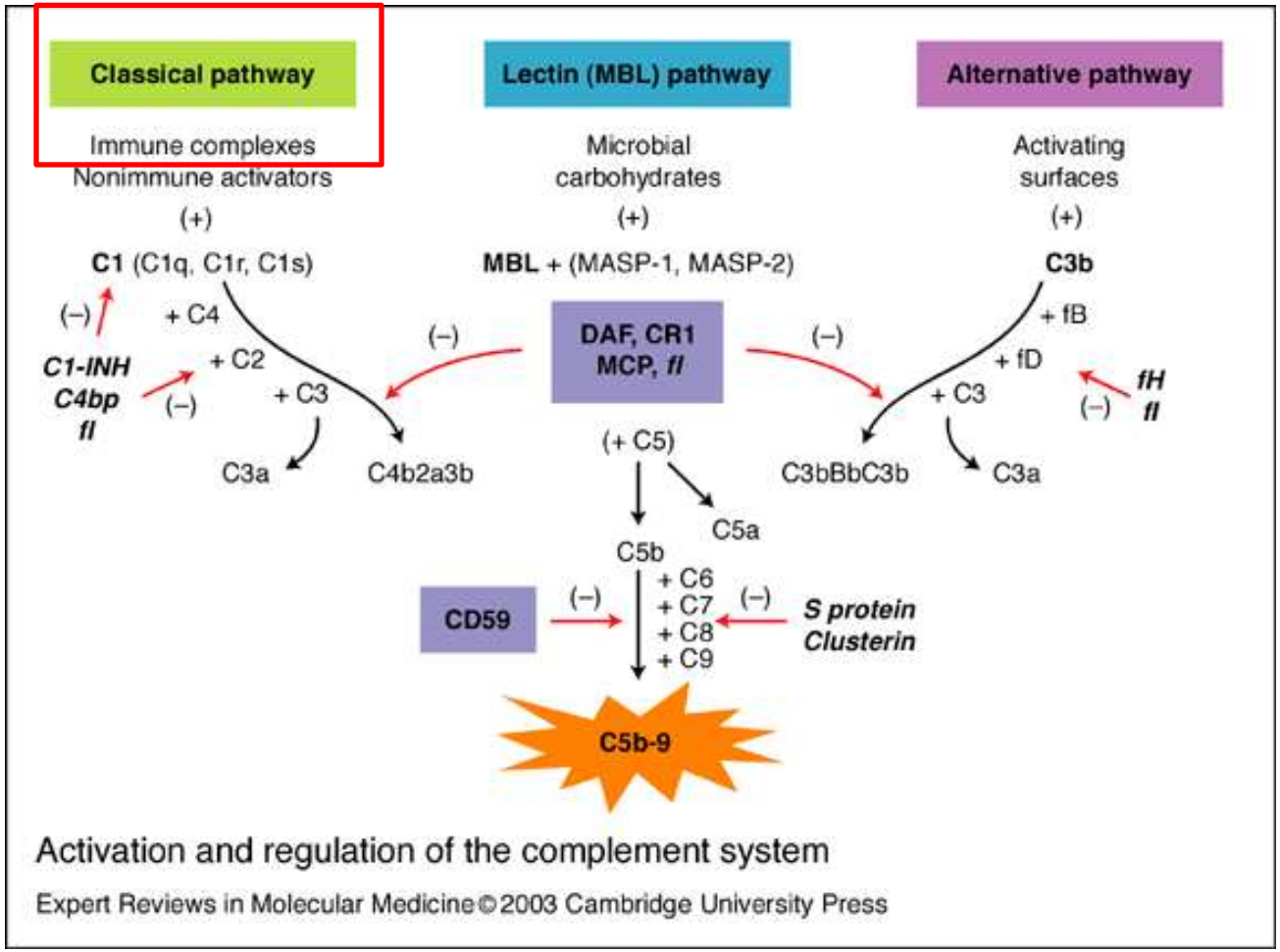

Activation and regulation of the complement system

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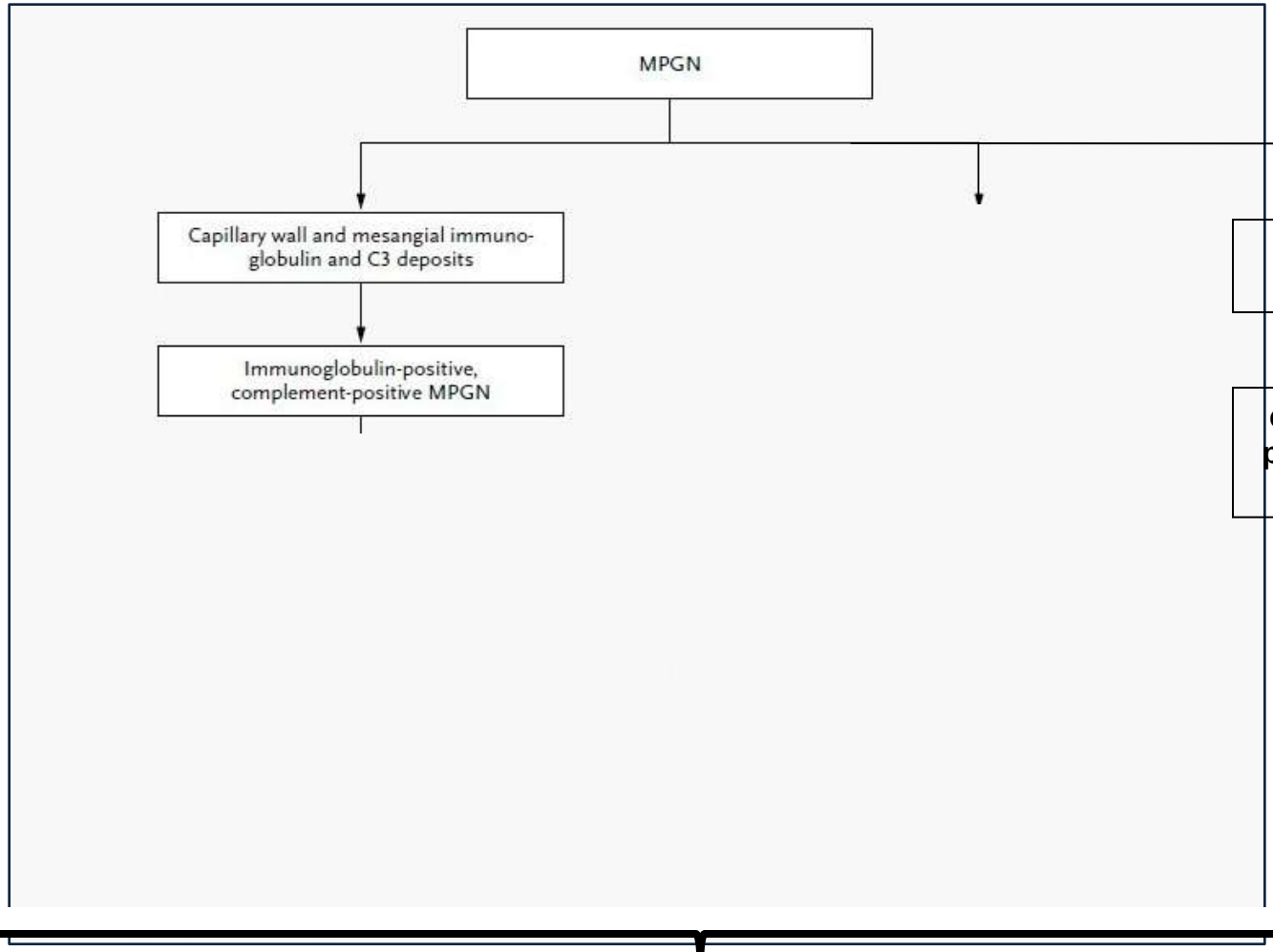
MPGN Classification

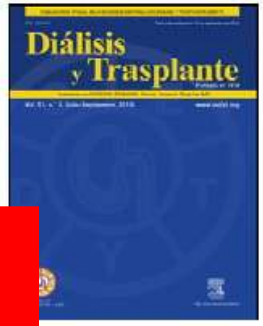
According to TYPE of deposits



Always check the possibility of Infection

Algorithm source: Sanjeev Sethi et al. N Engl J Med 2012;366:1119-31.

Diálisis y Trasplante



Always suspect infection whatever the type of the deposits

CLINICAL RE

Typhoid

Pavan Malle at V. Shah

Department of Nephrology, Lilavati Hospital and Research Centre, Mumbai, India

Received 16 June 2011; accepted 9 July 2011

NDT Plus (2008) 5: 319–321
doi: 10.1093/ndtplus/sfn098
Advance Access publication 4 July 2008

NDT PLUS

Suspect any organism as a cause of post infectious MPGN whenever there is an evidence of infection

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syndrome resolved within 6 months from presentation. Our case report suggests that MPGN presenting with nephrotic syndrome may have a relatively benign course when it is associated with an acute EBV infection.

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oedema but no elevation of jugular venous pressure. There was no rash and no peripheral lymphadenopathy, and examination was otherwise unremarkable.

Initial laboratory investigations revealed normal electrolytes, liver enzymes and excretory kidney function with

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